January 28, 2004

Dr. Mark A. Thomson
Manager, Toxicology & International Product Registration
Crompton Corporation
199 Benson Road
Middlebury, CT 06749

Dear Dr. Thomson:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 4,4'-oxydi(benzenesulphonohydrazide) posted on the ChemRTK HPV Challenge Program Web site on September 30, 2003. I commend Crompton Corporation for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Crompton advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-*S*-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
4,4'-Oxydi(benzenesulphonohydrazide)

Summary of EPA Comments

The sponsor, Crompton Corporation, submitted a test plan and robust summaries to EPA for 4,4'-Oxydi(benzenesulphonohydrazide) (CAS No. 80-51-3) dated August 27, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on September 30, 2003.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties and Environmental Fate. The submitter needs to provide measured water solubility and biodegradation data and recalculate its fugacity values using measured data.

2. Health Effects. Adequate data are available for acute toxicity for the purposes of the HPV Challenge Program. EPA agrees with the submitter's plan to conduct a combined reproductive/developmental test. The data submitted for repeated-dose and genetic toxicity endpoints are inadequate. The submitter needs to either provide additional information or conduct testing to adequately address these endpoints.

3. Ecological Effects. EPA disagrees with the submitter that adequate data are available for the ecological endpoints. Adequate experimental data are needed either from an analog(s) or from additional testing.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on 4,4'-oxydi(benzenesulphonohydrazide) Challenge Submission

Generic Comment

The submitter needs to provide the purity of the test material in the submission.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The data provided by the submitter for melting point, boiling point, vapor pressure, and partition coefficient are adequate for the purposes of the HPV Challenge Program.

Water solubility. The submitter provided an estimated water solubility of 4,733 mg/L at 25 °C for 4,4'-oxydi(benzenesulphonohydrazide); however, HPV Challenge Program guidelines indicate that testing be done for substances with an estimated water solubility greater than 1 µg/L. The submitter needs to provide measured water solubility data for this chemical.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data provided by the submitter for photodegradation and stability in water are adequate for the purposes of the HPV Challenge Program.

Biodegradation. The submitter provided estimated biodegradation data for 4,4'-oxydi(benzenesulphonohydrazide), which are not adequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured ready biodegradation data for this chemical following OECD TG 301.

Fugacity. The submitter needs to use the melting point and vapor pressure values reported in the robust summaries as inputs into the fugacity model. When measured data or data from peer reviewed literature are available, it is not recommended to use the default values in EPIWIN. The use of estimated values introduces uncertainties that then become magnified in modeling applications.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data are available for acute toxicity for the purposes of the HPV Challenge Program. The data submitted for repeated-dose and genetic toxicity endpoints are inadequate because they are from secondary sources and missing critical information. The submitter needs to obtain the original study reports to adequately address these endpoints, otherwise testing will be needed if existing data are not available. In addition, the submitter needs to provide additional information in one of the robust summaries.

Repeated-dose and genetic toxicity. The data submitted for these endpoints are inadequate because they are from secondary sources and missing critical information. For repeated-dose toxicity, the 90-day oral feed study and 4-month gavage study in rats omitted the purity of the test material, the strain of rats, the endpoints examined (hematology, clinical chemistry, urinalysis, gross pathology and histopathology), the magnitude of body, liver, and kidney weight changes, the incidences of compound-related lesions by dose and sex, and the organs or tissues that were examined for histopathology.

For genetic toxicity, the omitted information in the robust summaries for bacterial mutations and chromosomal aberrations includes the purity of the test material, the strains of bacteria used, the number of replicates per concentration, the cytotoxic concentrations, the positive and negative controls used for the gene mutations test, the number of colonies and/or metaphases per concentration that were examined, and the criteria for positive results.

Reproductive and developmental toxicity. EPA agrees with the submitter's plan to conduct a combined reproductive and developmental screening test following OECD TG 421. Since the data submitted for repeated-dose toxicity endpoint are not adequate, a combined repeated-dose/reproductive/developmental screening test (OECD TG 422) will be needed if additional information as indicated above is not available.

Ecological Effects (fish, invertebrates, and algae).

The submitter did not provide any experimental data. The submitter needs to provide data on an adequate analog(s) or conduct testing for all endpoints. Quantitative Structure Activity Relationship (QSAR) estimates are not reliable for this class of chemical.

Specific Comments on the Robust Summaries

Health Effects

Acute toxicity. A robust summary for an acute oral toxicity study in rats omitted the purity of the test material, tested doses, and systemic toxicity in target organs by dose and sex (if there is any).

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.